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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/508,759	09/22/2004	Hyo Jeong Hong	DE1586	9699

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EXAMINER	
BOESEN, AGNIESZKA	
ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/508,759	HONG ET AL.	
	Examiner	Art Unit	
	AGNIESZKA BOESEN	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-24* is/are pending in the application.

4a) Of the above claim(s) *11-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3,6,7,9 and 10* is/are rejected.

7)☒ Claim(s) *4, 5 and 8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 17, 2009 has been entered.

Claims 2 and 3 have been amended. Claims 2, 3-10 are under examination in this Office Action.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequence set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). See present Drawings which lack the SEQ ID NOs (particularly Figure 2b and 4b). Additionally the sequences provided by Applicant in Response of 2/17/2009 lack SEQ ID NOs or a computer readable form.

However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason (s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. The time for response to this Notice to Comply is the same as the time for response to the present Office Action, which is 3 months from mailing of this Office Action.

The addresses below are effective 5 June 2004. Please direct all replies to the United States Patent and Trademark Office via one (1) of the following:

1. Electronically submitted through EFS-Bio

(http://www.uspto.gov/ebc/efs/downloads/documents.htm,

EFS Submission user Manual – ePAVE)

2. Mailed to:

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P.O. Box 22313-1450

3. Hand Carry, Federal Express, United parcel Service or other

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Claim Rejections - 35 USC § 112

Rejection of claims 3 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of Applicant's amendment.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Rejection of claims 6, 7, 9 and 10 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement **is maintained**.

Applicant's arguments have been fully considered but fail to persuade. Applicant argues that the enclosed certificates indicating the deposit of hybridoma cell lines KCTC10198BP and KCTC10199BP substantiate the hybridoma cell lines for producing the claimed constructs.

In response, the Examiner notes that the certificates of deposit of hybridoma cell lines KCTC10198BP and KCTC10199BP are defective for the purposes of satisfying the Biological Deposit requirement. Applicant is directed to MPEP 2402. Particularly, if a deposit is not made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(a) during the pendency of this application, access to the invention will be afforded to one determined by the Commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(d) a viability statement in accordance with the provisions of 37 CFR 1.807; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803 - 37 CFR 1.809 for additional explanation of these requirements.

Applicant argues that in the last lines of Figure 2b and Figure 4b, JH4 of DP7-JH4 and JK4 of DPK12-JK4 are indicated respectively. Applicant also provided the sequences of DP7 and JH4. It is acknowledged that Applicant provided the sequences of DP7 and JH4 although the provided sequences lack sequence identifiers, as noted under Sequence compliance above. Additionally, the sequences of DPH12-JK4 are not provided in the present specification. Looking at Figures 2a-c and 2b it is not clear which sequences are the sequences for DPH12-JK4. Additionally, the sequences in Figures 2a-c and 2b lack SEQ ID NOs.

Figures 2a-c and 2b disclose the sequences of KR127 heavy and light chains. It is noted that KR127 is a murine antibody and DP7-JH4 or DPH12-JK4 are human antibodies heavy and light chain, respectively. As acknowledged in the Office action of March 18, 2008, the specification and the sequence listing provides SEQ ID NOs for the heavy and light chain of the KR127 antibody, however neither the specification nor the sequence listing provide the sequences of DP7-JH4 and DPH12-JK4.

In Remarks of June 18, 2008 Applicant points to Figures 2a-c and 2b however Applicant does not refer to any specific SEQ ID NOs encoding the DP7-JH4 or DPH12-JK4. The present sequence listing does not list SEQ ID NOs of the DP7-JH4 or DPH12-JK4, or the SEQ ID NO: of the KR127 that is grafted onto DP7-JH4 or DPH12-JK4. The disclosure of DP7, JH4, DPK12

and JK in the prior art is not sufficient to enable the skilled artisan to make and use the claimed antibodies, because it is unknown whether those human germline sequences have been made publicly available at the time of the invention. Only because the prior art references were publicly available at the time of the invention (as indicated by Applicant) that does not ensure the availability of the antibodies disclosed in the cited references. It is also noted that Applicant provides argument only with regard to the heavy chain DP7-JH4 recited in the claims, however Applicant dos not mention the light chain DPH12-JK4. It is noted that DPH12-JK4 and DPK-JK4 are not the same constructs. The specification discloses both DPH12-JK4 and DPK-JK4 (see page 5). It is understood that DPH12-JK4 and DPK-JK4 are two different light chains. However the DPH12-JK4 is recited in the present claims and there is no sequence, a vector or a hybridoma cell line producing the DPH12-JK4, and Applicant did not provide arguments with regard to the availability of DPH12-JK4. Thus because it would have been undue experimentation to practice the present invention without access to **DPH12-JK4**, and because Applicant did not provide sequences, vectors or a hybridoma cell lines producing the claimed constructs, the rejection is maintained.

Claim Rejections - 35 USC § 102

Rejection of claim 2 under 35 U.S.C. 102(b) as being anticipated by Leong et al. (Cytokine, November 2001, Vol. 16, p. 106-119) **is withdrawn** in view of Applicant's arguments.

New Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 2 is rejected under 35 U.S.C. 103(a) as being obvious over Leong et al. (Cytokine, November 2001, Vol. 16, p. 106-119).

Leong et al. teaches a method of preparing humanized anti-IL-8 antibody comprising performing alanine scanning mutagenesis of the murine CDRs in order to determine the specificity determining residies SDRs, comprising selecting alanine substituted amino acid positions that contribute to the binding to human IL-8 (thereby determining the specificity binding residues) and grafting the alanine substituted CDR regions of the murine anti-IL-8 antibody onto the human IgG framework (see the entire document, particularly Alanine scanning mutagenesis on page 108, Experimental procedures: Construction of humanized version of anti-IL-8 antibody 6G4.2.5, and Tables 1 and 2). It is noted that the step of "replacing each amino acid residue in the CDR region of murine monoclonal antibody" is commonly referred to in the art as: "alanine scanning mutagenesis". The present specification uses the term "alanine scanning mutagenesis" when discussing the steps of the present method (see [0026]). Leong discloses that his method step of alanine scanning mutagenesis is one of the method steps of making the humanized antibody (see Construction of humanized versions of anti-IL-8 antibody on page 107).

The difference between the Leong's method and the claimed method is that Leong is grafting the CDRs first and then performing the alanine scanning mutagenesis to determine the specificity determining regions (SDRs). It is noted that the present claim 2 does not require that step b) is necessarily done after step a), however Leong does not disclose grafting the SDRs as required by the present claims.

Absent any unexpected results, it would have been *prima facie* obvious to provide Leong's method wherein the alanine scanning mutagenesis, to determine the SDRs is performed prior to grafting the CDR. It would have been obvious to graft the SDRs as opposed to grafting the CDRs.

All the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Rejection of claim 3 under 35 U.S.C. 103(a) as being obvious over Maeng et al. (Virology, 2000 Vol. 270, p. 9-16) in view of Leong et al. (Cytokine, November 2001, Vol. 16, p. 106-119) **is maintained.**

Applicant's arguments have been fully considered but fail to persuade. Applicant argues that claim 2 has the novel step of grafting SDR among CDR. Claim 2 is now rejected under 35 U.S.C. 103(a) as being obvious over Leong et al.

As disused on the record, the process of making humanized antibodies according to the present claims has been known at the time of the invention, as taught by Leong. The murine KR127 monoclonal antibody has been known in the prior art, as taught by Maeng. Thus it would have been obvious to humanize KR127 antibody according to the method disclosed in Leong because the KR127 antibody has binding affinity for HBV pre-S1 antigen and humanizing murine KR127 antibody could have an application for human use.

Thus because the present claims would have been obvious to the skilled artisan at the time of the invention as discussed above and on the record, the rejection is maintained.

Claim Objection

Claims 4, 5, and 8 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AGNIESZKA BOESEN whose telephone number is (571)272-8035. The examiner can normally be reached on Monday through Friday from 9:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Agnieszka Boesen/

Examiner, Art Unit 1648